Alabama Medicaid DUR Board Meeting Minutes Summary
October 28, 2020

Members Present: Kelli Littlejohn Newman, Rachel Seaman, Crystal Deas, Kelly Tate, Bernie Olin, Clinton Martin, Jessica Jackson, Danielle Powell, Mary Stallworth, Melinda Rowe

Also Present: Lori Thomas, Clemice Hurst, Julie Jordan, Heather Vega, Jessica Flaherty, Alex Jenkins, Amy Donaldson, Lacy Miller, Emily Arnold, Lydia Rather, Kristian Testerman

Members Absent: Dan McConaghy

Call to Order: The DUR meeting was called to order by R. Seaman at approximately 1:01p.m.

Review and Adoption of Minutes: The minutes of the July 22, 2020 meeting were presented, and J. Jackson made a motion to approve the minutes. D. Powell seconded the motion, and the motion was approved unanimously.

Prior Authorization and Overrides Update: L. Thomas began the Prior Authorization and Overrides Update with the Monthly Manual Prior Authorizations and Overrides Report for the month of April 2020. She reported 10,635 total manual requests and 12,371 total electronic requests. From the Prior Authorization and Override Response Time Ratio report for April 2020, L. Thomas reported that approximately 92% of all manual PAs and all overrides were completed in less than two hours. Ninety-six percent of all manual PAs and all overrides were completed in less than four hours. Ninety-six percent of all manual PAs and 97% of all overrides were completed in less than eight hours. For the month of May 2020, L. Thomas reported 9,881 manual PA requests and 11,506 electronic PA requests were received. She reported that 95% of all manual PAs and 94% of all overrides were completed in less than two hours. Ninety-seven percent of all manual PAs and all overrides were completed in less than four hours. Ninety-eight percent of all manual PAs and all overrides were completed in less than eight hours. For the month of June 2020, L. Thomas reported 11,213 manual PA requests and 12,915 electronic PA requests. L. Thomas reported that approximately 86% of all manual PAs and all overrides were completed in less than two hours. Ninety-two percent of all manual PA requests and overrides were completed in less than four hours. Ninety-three percent of all manual PA requests and 94% of all overrides were completed in less than eight hours.

Program Summary Review: L. Thomas briefly reviewed the Alabama Medicaid Program Summary for the months of January 2020 through June 2020. She reported 3,395,612 total prescriptions, 205,250 average recipients per month using pharmacy benefits, and an average paid per prescription of $127.73.

Cost Management Analysis: L. Thomas reported an average cost per claim of $138.34 for June 2020 and emphasized that the table contained the average cost per claim over the past two years. From the 2nd Quarter 2020 Drug Analysis, L.Thomas reported 81% generic utilization, 9% brand single-source, 6% brand multi-source (those requests which required a DAW override), and 4% OTC and "other". From the Top 25 Drugs Based on Number of Claims from 04/01/2020 – 06/30/2020, L.Thomas reported the top five drugs: cetirizine, montelukast sodium, gabapentin, hydrocodone-acetaminophen, and fluticasone propionate. L. Thomas mentioned that although hydrocodone-acetaminophen moved into the top 5, the number of claims was still lower than 1st Quarter 2020. L. Thomas then reported the top five drugs from the Top 25 Drugs Based on Claims Cost from 04/01/2020 – 06/30/2020: Vyvanse®, Invega® Sustenna®, Focalin XR®, Suboxone®, and Humira® Citrate-free. From the Top 15 Therapeutic Classes by Total Cost of Claims for the same time frame, L.Thomas reported the top five classes: Antipsychotic Agents, Insulins, Disease-modifying Antirheumatic Agents, Miscellaneous Anticonvulsants, and Respiratory and CNS Stimulants.

Opioid Utilization: L. Thomas presented several charts showing override requests for opioids and opioid dependence medications. Trends were shown for the months of June and July 2018; June and July 2019; and June and July 2020. K. Newman continued the discussion reporting on opioid claims data. She also briefed the Board on the Morphine Milligram Equivalent (MME) edit that was phased in on May 1, 2019. The Board was presented with the option to continue phasing in the MME edit but declined at this time due to the COVID-19 pandemic.

RDUR Intervention Report: L. Thomas presented the RDUR Activity Report for April 2020. She reported 500 profiles reviewed and 801 letters sent with 98 responses received as of the date of the report. She reported 26 of 59 physicians indicated that they found the RDUR letters "useful" or "extremely useful". The criteria for the cycle of intervention letters included Drug-Drug Interaction (Support Act criteria – pure opioid agonists and benzodiazepines); Drug-Drug Interaction (Support Act criteria – pure opioid agonists and antipsychotics); Appropriate Use (concurrent use of buprenorphine and pure opiate agonists).

Proposed Criteria: L.Thomas presented the proposed set of 39 criteria to the Board and instructed the Board members to mark their ballots. Of the 39 proposed criteria, results from the criteria vote returned 38 approved and 1 approved as amended.

Medicaid Update: K. Newman reminded the Board members that all updated Medicaid drug lists and ALERTs were provided to them electronically and are also available online.

P & T Committee Update: C. Hurst began the P & T Update by informing the Board that the last meeting was held on August 5, 2020, and covered the Skeletal Muscle Relaxants; Opiate Agonists; Opiate Partial Agonists; Selective Serotonin Agonists; Antiemetics; Proton Pump Inhibitors; and Antimigraine Agents. The next P & T Committee meeting will be held on November 4, 2020 and will cover the Alzheimer's Agents; Antidepressants; Cerebral Stimulants; Wakefulness Promoting Agents; Anxiolytics, Sedatives, and Hypnotics; Genitourinary Smooth Muscle Relaxants; and Disease-Modifying Antirheumatic Agents.

Next Meeting Date: The next DUR Board meeting will be held on January 27, 2021. A motion to adjourn the meeting was made by B. Olin. K. Tate seconded the motion and the meeting was adjourned at 1:56 p.m.

Respectfully submitted,

Lori Thomas, PharmD

Lori Thomas, PharmD.

ALABAMA MEDICAID
RETROSPECTIVE DRUG UTILIZATION REVIEW
CRITERIA RECOMMENDATIONS

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*
1. Lumateperone / Overuse Alert Message: Caplyta (lumateperone) may be over-utilized. The recommended daily dose of lumateperone for adult patients with schizophrenia is 42 mg orally once daily with food. Drugs/Diseases Util A: Lumateperone Util B: Util C: Max Dose: 42 mg/day References: Clinical Pharmacology, 2020 Elsevier/Gold Standard. Facts & Comparisons, 2020 Updates, Wolters Kluwer Health. Caplyta Prescribing Information, Dec. 2019, Intra-Cellular Therapies, Inc.	√		
2. Lumateperone / Therapeutic Appropriateness Alert Message: The safety and effectiveness of Caplyta (lumateperone) have not been established in pediatric patients. Drugs/Diseases Util A: Lumateperone Util B: Util C: Age Range: 0 – 17 yoa References: Clinical Pharmacology, 2020 Elsevier/Gold Standard. Facts & Comparisons, 2020 Updates, Wolters Kluwer Health. Caplyta Prescribing Information, Dec. 2019, Intra-Cellular Therapies, Inc.	√		
3. Lumateperone / Cirrhosis Alert Message: The use of Caplyta (lumateperone) should be avoided in patients with moderate to severe hepatic impairment (Child-Pugh B or C). Patients with moderate to severe hepatic impairment experience higher exposure to lumateperone and are at increased risk for lumateperone-related adverse reactions. No dosage adjustment is recommended for patients with mild hepatic impairment (Child-Pugh A). Drugs/Diseases Util A: Lumateperone Util B: Cirrhosis Util C: References: Clinical Pharmacology, 2020 Elsevier/Gold Standard. Facts & Comparisons, 2020 Updates, Wolters Kluwer Health. Caplyta Prescribing Information, Dec. 2019, Intra-Cellular Therapies, Inc.	√		

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

4. Lumateperone / Tardive Dyskinesia ___√___ _____ _____

Alert Message: Like other antipsychotics, Caplyta (lumateperone) may cause tardive dyskinesia. Lumateperone should be prescribed in a manner to most likely reduce the risk of tardive dyskinesia, i.e., using the lowest dose and for the shortest duration of treatment producing a satisfactory clinical response. If signs and symptoms of tardive dyskinesia appear, drug discontinuation should be considered.

Drugs/Diseases

Util A	Util B	Util C
Lumateperone	Tardive Dyskinesia	

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Facts & Comparisons, 2020 Updates, Wolters Kluwer Health.
Caplyta Prescribing Information, Dec. 2019, Intra-Cellular Therapies, Inc.

5. Lumateperone / Seizures ___√___ _____ _____

Alert Message: Caplyta (lumateperone) should be used with caution in patients with a history of seizures or with conditions that lower the seizure threshold. Like other antipsychotics, lumateperone may cause seizures. Conditions that lower the seizure threshold may be more prevalent in older patients.

Drugs/Diseases

Util A	Util B	Util C
Lumateperone	Seizures	
	Epilepsy	
	Stroke	
	Head Trauma	
	Intracranial infection	
	Anorexia Nervosa	
	Meningitis	

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Caplyta Prescribing Information, Dec. 2019, Intra-Cellular Therapies, Inc.
Oh CY and Bainbridge J. Lowering the Seizure Threshold Associated with Antidepressants, Stimulants, Antipsychotics, and Others. Mental Health Clinician: Nov. 2012, Vol 2, No. 5, pp.127 – 128.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

6. Lumateperone / CYP3A4 Inducers ___√___ _____ _____

Alert Message: The concurrent use of Caplyta (lumateperone) with CYP3A4 inducers should be avoided. Lumateperone is a CYP3A4 substrate, and coadministration with a CYP3A4 inducer may result in decreased lumateperone exposure and loss of efficacy.

Drugs/Diseases

Util A	Util B	Util C
Lumateperone	Apalutamide	Bosentan
	Carbamazepine	Efavirenz
	Enzalutamide	Etravirine
	Lumacaftor	Dexamethasone
	Mitotane	Modafinil
	Phenobarbital	
	Phenytoin	
	Primidone	
	Rifabutin	
	Rifampin	
	Rifapentine	

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Facts & Comparisons, 2020 Updates, Wolters Kluwer Health.

7. Lumateperone / Moderate to Strong CYP3A4 Inhibitors ___√___ _____ _____

Alert Message: The concurrent use of Caplyta (lumateperone) with CYP3A4 inhibitors should be avoided. Lumateperone is a CYP3A4 substrate, and coadministration with a CYP3A4 inhibitor may result in increased lumateperone exposure and risk of lumateperone-related adverse reactions.

Drugs/Diseases

Util A	Util B	Util C
Lumateperone	Atazanavir	Aprepitant
	Clarithromycin	Cimetidine
	Cobicistat	Ciprofloxacin
	Idelalisib	Clotrimazole
	Indinavir	Crizotinib
	Itraconazole	Cyclosporine
	Ketoconazole	Diltiazem
	Nefazodone	Dronedarone
	Nelfinavir	Erythromycin
	Posaconazole	Fluconazole
	Ritonavir	Fluvoxamine
	Saquinavir	Fosamprenavir
	Tipranavir	Verapamil
	Voriconazole	

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Facts & Comparisons, 2020 Updates, Wolters Kluwer Health.
Caplyta Prescribing Information, Dec. 2019, Intra-Cellular Therapies, Inc.
FDA: Drug Development and Drug Interactions: Tables of Substrates, Inhibitors, and Inducers. Available at:
http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/DrugInteractionaLabeling/ucm093664.htm

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

8. Lumateperone / UGT Inhibitors ___√_____ _____ _____

Alert Message: The concurrent use of Caplyta (lumateperone) with UGT inhibitors should be avoided. Lumateperone is a UGT substrate, and coadministration with a UGT inhibitor may result in increased lumateperone exposure and risk of lumateperone-related adverse reactions.

Drugs/Diseases

Util A	Util B	Util C
Lumateperone	Probenecid	
	Valproic Acid	

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Facts & Comparisons, 2020 Updates, Wolters Kluwer Health.
Caplyta Prescribing Information, Dec. 2019, Intra-Cellular Therapies, Inc.
FDA: Drug Development and Drug Interactions: Tables of Substrates, Inhibitors, and Inducers. Available at: http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/DrugInteractionaLabeling/ucm093664.htm

9. Lumateperone / Lactation (Females 11 – 50 yoa) ____√_____ _____ _____

Alert Message: Based on findings of toxicity in animal studies and the potential for serious adverse reactions in the breastfed infant, breastfeeding is not recommended during treatment with Caplyta (lumateperone). There are no available data on the presence of lumateperone or its metabolites in human milk, the effects on the breastfed infant, or the effects on milk production.

Drugs/Diseases

Util A	Util B	Util C
Lumateperone	Lactation	

Age Range: 11 – 50 yoa
Gender: Female

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Caplyta Prescribing Information, Dec. 2019, Intra-Cellular Therapies, Inc.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

10. Lumateperone / Non-adherence ___√_____ _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Caplyta (lumateperone). Nonadherence to the prescribed dosing regimen may result in sub-therapeutic effects, which may lead to decreased patient outcomes and additional healthcare costs.

Drugs/Diseases

Util A	Util B	Util C
Lumateperone		

References:

Theida P, et.al., An Economic Review of Compliance with Medication Therapy in the Treatment of Schizophrenia, Psychiatric Services, 2003;54:508-516.

Acsher-Svanum H, Zhu B, Faries DE, et al., The Cost of Relapse and the Predictors of Relapse in the Treatment of Schizophrenia. BMC Psychiatry 2010, 10:2.

Berger A, Edelsbery J, Sanders KN, et al., Medication Adherence and Utilization in Patients with Schizophrenia or Bipolar Disorder Receiving Aripiprazole, Quetiapine, or Ziprasidone at Hospital Discharge: A Retrospective Cohort Study. BMC Psychiatry 2012,12:99.

Stephenson JJ, Tuncelli O, Gu T, et al., Adherence to Oral Second-Generation Antipsychotic Medications in Patients with Schizophrenia and Bipolar Disorder: Physicians' Perceptions of Adherence vs. Pharmacy Claims. Int J Clin Pract, June 2012, 66, 6, 565-573.

Morken G, Widen JH, Grawe RW. Non-adherence to Antipsychotic Medication, Relapse, and Rehospitalisation in Recent-Onset Schizophrenia. BMC Psychiatry. 2008, 8:32.

11. Voxelotor / Overuse ___√_____ _____ _____

Alert Message: Oxbryta (voxelotor) may be over-utilized. The recommended maximum daily dose of voxelotor in adults and pediatric patients 12 years of age and older is 1500 mg once daily with or without food.

Drugs/Diseases

Util A	Util B	Util C **(Negate)**
Voxelotor		Cirrhosis
		Strong or Moderate CYP3A4 Inducers
		Strong CYP3A4 Inhibitors & Fluconazole

Max Dose: 1500 mg/day

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.

Oxbryta Prescribing Information, Nov. 2019, Global Blood Therapeutics, Inc.

12. Voxelotor / Overuse – Hepatic Impairment ___√_____ _____ _____

Alert Message: Oxbryta (voxelotor) may be over-utilized. The recommended dosage of voxelotor in patients with severe hepatic impairment (Child-Pugh C) is 1,000 mg taken once daily with or without food. No dosage adjustment of voxelotor is required for patients with mild or moderate hepatic impairment.

Drugs/Diseases

Util A	Util B	Util C **(Include)**
Voxelotor		Cirrhosis

Max Dose: 1000 mg/day

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.

Oxbryta Prescribing Information, Nov. 2019, Global Blood Therapeutics, Inc.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

13. Voxelotor / Strong CYP3A4 Inhibitors & Fluconazole ___√_____ _____ _____

Alert Message: The co-administration of Oxbryta (voxelotor) with strong CYP3A4 inhibitors or fluconazole should be avoided due to the increased risk of voxelotor toxicity. If concurrent use is warranted, decrease the voxelotor dosage to 1000 mg once daily.

Drugs/Diseases

Util A	Util B	Util C **(Include)**	
Voxelotor		Cobicistat	Nelfinavir
		Clarithromycin	Nefazodone
		Fluconazole	Posaconazole
		Indinavir	Ritonavir
		Itraconazole	Saquinavir
		Ketoconazole	Voriconazole

Max Dose: 1000 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Oxbryta Prescribing Information, Nov. 2019, Global Blood Therapeutics, Inc.

14. Voxelotor / Moderate & Strong CYP3A4 Inducers ___√_____ _____ _____

Alert Message: The co-administration of Oxbryta (voxelotor) with moderate or strong CYP3A4 inducers should be avoided. Concurrent use of these agents with voxelotor, a CYP3A4 substrate, may result in decreased voxelotor plasma concentrations and loss of efficacy. If concurrent use is warranted, increase the voxelotor dosage to 2500 mg once daily.

Drugs/Diseases

Util A	Util B		Util C
Voxelotor	Bosentan	Mitotane	Rifapentine
	Butabarbital	Modafinil	
	Carbamazepine	Nevirapine	
	Dexamethasone	Phenobarbital	
	Enzalutamide	Phenytoin	
	Efavirenz	Primidone	
	Etravirine	Rifabutin	
		Rifampin	

Max Dose: 2500 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Oxbryta Prescribing Information, Nov. 2019, Global Blood Therapeutics, Inc.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

15. Voxelotor / Sensitive CYP3A4 Substrates w/ NTI ___√_____ _____ _____

Alert Message: The co-administration of Oxbryta (voxelotor) with sensitive CYP3A4 substrates with a narrow therapeutic index should be avoided. In vivo drug studies have shown that concurrent use of voxelotor, a weak CYP3A4 inhibitor, with midazolam resulted in increased midazolam exposure by 1.6-fold and the predicted increase in patients after multiple dosing is 2-fold. If concomitant use is unavoidable, consider a dose reduction of the sensitive CYP3A4 substrate(s).

Drugs/Diseases

Util A	Util B				Util C
Voxelotor	Avanafil	Eletriptan	Lurasidone	Simvastatin	Vardenafil
	Budesonide	Eplerenone	Maraviroc	Sirolimus	
	Buspirone	Everolimus	Midazolam	Tacrolimus	
	Carbamazepine	Felodipine	Naloxegol	Ticagrelor	
	Darifenacin	Ibrutinib	Nisoldipine	Tipranavir	
	Darunavir	Lomitapide	Quetiapine	Tolvaptan	
	Dronedarone	Lovastatin	Sildenafil	Triazolam	

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Oxbryta Prescribing Information, Nov. 2019, Global Blood Therapeutics, Inc.
1398 / FDA: Drug Development and Drug Interactions: Tables of Substrates, Inhibitors, and Inducers. Available at: http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/DrugInteractionaLabeling/ucm093664.htm

16. Voxelotor / Therapeutic Appropriateness ___√_____ _____ _____

Alert Message: The safety and effectiveness of Oxbryta (voxelotor) for sickle cell disease have been established in pediatric patients aged 12 years and older.

Drugs/Diseases

Util A	Util B	Util C
Voxelotor		

Age Range: 0 – 11 yoa

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Oxbryta Prescribing Information, Nov. 2019, Global Blood Therapeutics, Inc.

17. Voxelotor / Pregnancy / Pregnancy Negating (Females 11 – 50 yoa) ___√_____ _____ _____

Alert Message: There are no available data on Oxbryta (voxelotor) use in pregnant women to evaluate for a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. Voxelotor should only be used during pregnancy if the benefit of the drug outweighs the potential risk.

Drugs/Diseases

Util A	Util B	Util C **(Negating)**
Voxelotor	Pregnancy	Abortion
		Delivery
		Miscarriage

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Oxbryta Prescribing Information, Nov. 2019, Global Blood Therapeutics, Inc.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

18. Voxelotor / Lactation (Females 11 – 50 yoa) ___√_____ _____ _____

Alert Message: There are no data on the presence of Oxbryta (voxelotor) in human milk, the effects on the breastfed child, or the effects on milk production. Because of the potential for serious adverse reactions in the breastfed child, including changes in the hematopoietic system, advise patients that breastfeeding is not recommended during treatment with voxelotor, and for at least 2 weeks after the last dose.

Drugs/Diseases

Util A	Util B	Util C
Voxelotor	Lactation	

Age Range: 11 – 50 yoa
Gender: Female

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Oxbryta Prescribing Information, Nov. 2019, Global Blood Therapeutics, Inc.

19. CDK 4/6 Inhibitors / ILD Symptoms and Interstitial Pneumonitis ___√_____ _____ _____

Alert Message: Severe, life-threatening, or fatal interstitial lung disease (ILD) and/or pneumonitis can occur in patients treated with CDK 4/6 inhibitors (abemaciclib, palbociclib, and ribociclib). Monitor patients for pulmonary symptoms indicative of ILD/pneumonitis. Symptoms may include hypoxia, cough, dyspnea, or interstitial infiltrates on radiologic exams. Dose interruption or dose reduction is recommended for patients who develop persistent or recurrent Grade 2 ILD/pneumonitis. Permanently discontinue the CDK 4/6 inhibitor in all patients with Grade 3 or 4 ILD or pneumonitis.

Drugs/Diseases

Util A	Util B	Util C
Abemaciclib	Acute Interstitial Pneumonitis	
Palbociclib	Cough	
Ribociclib	Dyspnea	
	Fever	
	Hypoxemia	

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
US Food & Drug Administration. FDA Drug Safety Communications. FDA Warns About Rare But Severe Lung Inflammation with Ibrance, Kisqali, and Verzenio for Breast Cancer. Safety Announcement. [09-13-2019]. Available at: https://www.fda.gov/drugs/drug-safety-and-availability/fda-warns-about-rare-severe-lung-inflammation-ibrance-kisqali-and-verzenio-breast-cancer.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

20. Statins / Lactation (Females 11 – 50 yoa) ___√_____ _____ _____

Alert Message: HMG-CoA reductase inhibitors (statins) are contraindicated in breastfeeding women. Because of the potential for serious adverse reactions in a breastfed infant, advise patients that breastfeeding is not recommended during treatment with statins.

Drug/Disease:

Util A	Util B	Util C
Atorvastatin	Lactation	
Fluvastatin		
Lovastatin		
Pitavastatin		
Pravastatin		
Rosuvastatin		
Simvastatin		

Age Range: 11 – 50 yoa
Gender: Female

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Facts & Comparisons, 2020 Updates, Wolters Kluwer Health.

21. Semaglutide Tabs / Overuse ___√_____ _____ _____

Alert Message: Rybelsus (semaglutide) may be over-utilized. The recommended maximum daily dose of oral semaglutide is 14 mg once daily.

Drugs/Diseases

Util A	Util B	Util C
Semaglutide Tabs		

Max Dose: 14 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Rybelsus Prescribing Information, Jan. 2020, Novo Nordisk, Inc.

22. Semaglutide Tabs / Non-adherence ___√_____ _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Rybelsus (semaglutide). Nonadherence to the prescribed dosing regimen may result in sub-therapeutic effects, which may lead to decreased outcomes and additional healthcare costs.

Drugs/Diseases

Util A	Util B	Util C
Semaglutide Tabs		

References:
Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005; 353:487- 497.
Ho PM, Rumsfeld JS, Masoudi FA, et al., Effect of Medication Nonadherence in Diabetes Mellitus. Cardiology Review, April 2007.
Currie CJ, Peyrot M, Morgan CL, et al. The Impact of Treatment Noncompliance on Mortality in People With Type 2 Diabetes. Diabetes Care 35:1279-1284, June 2012.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

23. Semaglutide Tabs / Medullary Thyroid Carcinoma & MEN 2 ___√_____ _____ _____

Alert Message: The use of Rybelsus (semaglutide), a glucagon-like peptide-1 (GLP-1) receptor agonist, is contraindicated in patients with a personal or family history of medullary thyroid carcinoma (MTC) or with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). GLP-1 receptor agonists have been shown to increase the incidence of thyroid C-cell tumors in rodents. Patients should be counseled regarding the risk of MTC and the symptoms of thyroid tumors (e.g., a mass in the neck, dysphagia, dyspnea, or persistent hoarseness).

Drugs/Diseases

Util A	Util B	Util C **(Include)**
Semaglutide Tabs		Medullary Thyroid Carcinoma II
		Thyroid Carcinoma
		History of Thyroid Carcinoma

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Rybelsus Prescribing Information, Jan. 2020, Novo Nordisk, Inc.

24. Semaglutide Tabs / Therapeutic Appropriateness ___√_____ _____ _____

Alert Message: Rybelsus (semaglutide) is a glucagon-like peptide-1 (GLP-1) receptor agonist and GLP-1 receptor agonists have been shown to cause thyroid C-cell tumors at clinically relevant exposure in rodents. It is unknown whether semaglutide causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans. Patients should be counseled regarding the risk of medullary thyroid carcinoma and the symptoms of thyroid tumors (e.g., a mass in the neck, dysphagia, dyspnea, or persistent hoarseness).

Drugs/Diseases

Util A	Util B	Util C
Semaglutide Tabs		

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Rybelsus Prescribing Information, Jan. 2020, Novo Nordisk, Inc.

25. Semaglutide Tabs / Pancreatitis ___√_____ _____ _____

Alert Message: In clinical trials, acute pancreatitis has been reported in association with Rybelsus (semaglutide) use. If pancreatitis is suspected, semaglutide should be discontinued promptly. If confirmed, semaglutide should not be restarted. Semaglutide has not been studied in patients with a history of pancreatitis to determine whether these patients are at increased risk for pancreatitis. Consider other antidiabetic therapies in patients with a history of pancreatitis.

Drugs/Diseases

Util A	Util B	Util C
Semaglutide Tabs	Pancreatitis	

References:
Clinical Pharmacology, 2018 Elsevier/Gold Standard.
Rybelsus Prescribing Information, Jan. 2020, Novo Nordisk, Inc.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

26. Semaglutide Tabs / Diabetic Retinopathy ___√___ _____ _____

Alert Message: Patients with a history of diabetic retinopathy should be monitored for the progression of diabetic retinopathy when taking Rybelsus (semaglutide). In a pooled analysis of glycemic control trials with oral semaglutide, diabetic retinopathy complications occurred in 4.2% of patients receiving semaglutide and 3.8% with a comparator. Counsel patients to contact their physician if changes in vision are experienced during treatment with semaglutide.

Drugs/Diseases

Util A	Util B	Util C
Semaglutide Tabs	Diabetic Retinopathy	

References:
Clinical Pharmacology, 2018 Elsevier/Gold Standard.
Rybelsus Prescribing Information, Jan. 2020, Novo Nordisk, Inc.

27. Semaglutide Tabs / Therapeutic Appropriateness ___√___ _____ _____

Alert Message: The safety and effectiveness of Rybelsus (semaglutide) have not been established in pediatric patients (younger than 18 years).

Drugs/Diseases

Util A	Util B	Util C
Semaglutide Tabs		

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Rybelsus Prescribing Information, Jan. 2020, Novo Nordisk, Inc.

28. Semaglutide Tabs / Insulin and Insulin Secretagogues ___√___ _____ _____

Alert Message: The risk of hypoglycemia is increased when Rybelsus (semaglutide) is used in combination with insulin secretagogues (e.g., sulfonylureas) or insulin. Therefore, patients may require a lower dose of sulfonylurea or insulin to reduce the risk of hypoglycemia in this setting.

Drugs/Diseases

Util A	Util B	Util C
Semaglutide Tabs	Insulins	
	Chlorpropamide	
	Glimepiride	
	Glipizide	
	Glyburide	
	Tolazamide	
	Tolbutamide	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Rybelsus Prescribing Information, Jan. 2020, Novo Nordisk, Inc.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

29. Semaglutide Tabs / Oral Drugs w/NTI ___√___ _____ _____

Alert Message: Rybelsus (semaglutide) causes a delay of gastric emptying, and thereby has the potential to impact the absorption of other oral medications. When coadministering oral medications instruct patients to follow closely semaglutide administration instructions. Consider increased clinical or laboratory monitoring for medications that have a narrow therapeutic index or that require clinical monitoring.

Drugs/Diseases

Util A	Util B		Util C
Semaglutide Tabs	Carbamazepine	Phenytoin	
	Cyclosporine	Procainamide	
	Digoxin	Tacrolimus	
	Ethosuximide	Theophylline	
	Levothyroxine	Warfarin	
	Lithium		

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Rybelsus Prescribing Information, Jan. 2020, Novo Nordisk, Inc.

30. Semaglutide Tabs / Renal Impairment ___√___ _____ _____

Alert Message: There have been postmarketing reports of acute kidney injury and worsening of chronic renal failure, which may sometimes require hemodialysis, in patients treated with GLP-1 receptor agonists, including Rybelsus (semaglutide). Some of these events have been reported in patients without known underlying renal disease. A majority of the reported events occurred in patients who had experienced nausea, vomiting, diarrhea, or dehydration. Monitor renal function when initiating or escalating doses of semaglutide in patients reporting severe adverse gastrointestinal reactions.

Drugs/Diseases

Util A	Util B	Util C
Semaglutide Tabs	Renal Impairment	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Rybelsus Prescribing Information, Jan. 2020, Novo Nordisk, Inc.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

31. Semaglutide Tabs / Pregnancy / Delivery, Miscarriage & Abortion ___√_____ _____ _____

Alert Message: Available data with Rybelsus (semaglutide) use in pregnant women are insufficient to evaluate for a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. There are clinical considerations regarding the risks of poorly controlled diabetes in pregnancy. Based on animal reproduction studies, there may be potential risks to the fetus from exposure to semaglutide during pregnancy. Semaglutide should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Drugs/Diseases

Util A	Util B	Util C **(Negating)**
Semaglutide Tabs	Pregnancy	Delivery
		Miscarriage
		Abortion

Age Range: 11 – 50 yoa
Gender: Female

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Rybelsus Prescribing Information, Jan. 2020, Novo Nordisk, Inc.

32. Semaglutide Tabs / Lactation (Females 11 – 50 yoa) ___√_____ _____ _____

Alert Message: Rybelsus (semaglutide) use is not recommended in patients who are breast-feeding. While there are no data on the presence of semaglutide in human milk, semaglutide and salcaprozate sodium (an absorption enhancer in the oral product) has been shown to be present in the milk of lactating rats. When a substance is present in animal milk, the substance will likely be present in human milk. Other hypoglycemic agents may be considered as possible alternatives for treatment.

Drugs/Diseases

Util A	Util B	Util C
Semaglutide Tabs	Lactation	

Age Range: 11 – 50 yoa
Gender: Female

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Rybelsus Prescribing Information, Jan. 2020, Novo Nordisk, Inc.

33. Lasmiditan / Overuse ___√_____ _____ _____

Alert Message: Reyvow (lasmiditan) may be over-utilized. The maximum dose of lasmiditan is 200 mg. The recommended dose of lasmiditan is 50 mg, 100 mg, or 200 mg taken orally, as needed. No more than one dose should be taken in a 24 hour period. A second dose of lasmiditan has not been shown to be effective for the same migraine attack. The safety of treating more than 4 migraine attacks in a 30-day period has not been established.

Drugs/Diseases

Util A	Util B	Util C
Lasmiditan		

Max Dose: 200 mg/day

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Reyvow Prescribing Information, Oct. 2019, Eli Lilly and Company.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

34. Lasmiditan / Therapeutic Appropriateness ___√_____ _____ _____

Alert Message: The safety and effectiveness of Reyvow (lasmiditan) in pediatric patients have not been established.

Drugs/Diseases

Util A	Util B	Util C
Lasmiditan		

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Reyvow Prescribing Information, Oct. 2019, Eli Lilly and Company.

35. Lasmiditan / Therapeutic Appropriateness ___√_____ _____ _____

Alert Message: Reyvow (lasmiditan) has not been studied in patients with severe hepatic impairment (Child-Pugh C), and its use in these patients is not recommended.

Drugs/Diseases

Util A	Util B	Util C
Lasmiditan	Cirrhosis	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Reyvow Prescribing Information, Oct. 2019, Eli Lilly and Company.

36. Lasmiditan / CNS Depressants _____ ___√_____ _____

Alert Message: Reyvow (lasmiditan) can cause central nervous system (CNS) depression, including dizziness and sedation. Because of the potential for lasmiditan to cause sedation, other cognitive and/or neuropsychiatric adverse reactions, and driving impairment, lasmiditan should be used with caution if used in combination with alcohol or other CNS depressants.

Drugs/Diseases

Util A	Util B	Util C
Lasmiditan	Anticonvulsants	
	Antidepressants	
	Antihistamines	
	Antipsychotics	
	Barbiturates	
	Benzodiazepines	
	Cannabidiol	
	Muscle Relaxants	
	Narcotics	
	Sedative/Hypnotics	

References:
Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Reyvow Prescribing Information, Oct. 2019, Eli Lilly and Company.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*

37. Lasmiditan / Serotonergic Agents ___√_____ _____ _____

Alert Message: Caution should be exercised when Reyvow (lasmiditan) is co-administered with drugs that increase serotonin (i.e., SSRIs, SNRIs, TCAs, and MAOIs) due to the increased risk for serotonin syndrome. In clinical trials, the use of lasmiditan (a 5-HT1F receptor agonist) has been associated with reactions consistent with serotonin syndrome. Lasmiditan should be discontinued if serotonin syndrome is suspected.

Drugs/Diseases

Util A	Util B	Util C
Lasmiditan	Buspirone	
	Bupropion	
	Fentanyl	
	Linezolid	
	MAOIs	
	Meperidine	
	SNRIs	
	SSRIs	
	TCA's	
	Trazodone	
	Tramadol	
	Triptans	

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Reyvow Prescribing Information, Oct. 2019, Eli Lilly and Company.

38. Lasmiditan / Heart Rate Lowering Drugs ___√_____ _____ _____

Alert Message: Caution should be exercised when Reyvow (lasmiditan) is co-administered with drugs that lower heart rate, due to the risk of decreased heart rate. In clinical trials, lasmiditan use was associated with a mean decrease in heart rate of 5 to 10 beats per minute (bpm).

Drugs/Diseases

Util A	Util B		Util C
Lasmiditan	Amiodarone	Flecainide	Thalidomide
	Beta Blockers	Galantamine	
	Brigatinib	Ivabradine	
	Carbamazepine	Lacosamide	
	CCBs	Lanreotide	
	Ceritinib	Lithium	
	Clonidine	Mexiletine	
	Crizotinib	Pasireotide	
	Digoxin	Procainamide	
	Disopyramide	Propafenone	
	Donepezil	Quinidine	
	Dronedarone	Rivastigmine	
	Fingolimod	Siponimod	

References:

Clinical Pharmacology, 2020 Elsevier/Gold Standard.
Reyvow Prescribing Information, Oct. 2019, Eli Lilly and Company.

Criteria Recommendations	*Accepted*	*Approved As Amended*	*Rejected*
39. Lasmiditan / P-gp and BCRP Substrates	___v_____	_____	_____

Alert Message: Concomitant use of Reyvow (lasmiditan) and drugs that are P-gp or BCRP substrates should be avoided. Lasmiditan has been shown to inhibit P-gp and BCRP transport in vitro. Concurrent use of lasmiditan with these substrates would be expected to decrease substrate exposure and efficacy.

Drugs/Diseases

Util A	Util B	Util C
Lasmiditan	Afatinib	Methotrexate
	Apixaban	Morphine
	Aliskiren	Nilotinib
	Alpelisib	Quinidine
	Ambrisentan	Paliperidone
	Canagliflozin	Pazopanib
	Colchicine	Pibrentasvir
	Dabigatran	Prazosin
	Digoxin	Ranolazine
	Dolutegravir	Rivaroxaban
	Edoxaban	Rosuvastatin
	Empagliflozin	Saxagliptin
	Erythromycin	Sirolimus
	Everolimus	Sitagliptin
	Fexofenadine	Sulfasalazine
	Fluvastatin	Talazoparib
	Gefitinib	Tenofovir
	Glyburide	Topotecan
	Imatinib	Verapamil
	Indinavir	
	Lapatinib	
	Loperamide	
	Maraviroc	

References:

Reyvow Prescribing Information, Oct. 2019, Eli Lilly and Company.

Lee CA, O'Connor MA, Ritchie TK, et al., Breast Cancer Resistance Protein (ABCG2) in Clinical Pharmacokinetics and Drug Interactions: Practical Recommendations for Clinical Victim and Perpetrator Drug-Drug Interaction Study Design. Drug Metab Dispos. 2015 Apr;43(4):490-509. doi:10.1124/dmd.114.062174.

Stephanie McGee Azar, Commissioner — (✓) Approve ( ) Deny — 12-8-2020 Date

Melinda G. Rowe, MD, MBA, MPH
Assistant Medical Director — (✓) Approve ( ) Deny — 11/30/2020 Date

Kathy Hall, Deputy Commissioner — (✓) Approve ( ) Deny — Nov. 30, 2020 Date